DRAFT IL 12-2001-

MEDICAL RESEARCH SERVICE CLINICAL RESEARCH PROGRAM

1. The Veterans Health Administration Office of Research and Development, Medical Research Service (MRS) announces the initiation of the Clinical Research Program.

2. The Clinical Research Program is intended to promote investigator-initiated clinical research studies and to ensure that these studies receive appropriate consideration and evaluation.

a. For the purposes of this program, clinical research is defined as studies, involving veterans as research participants, designed to assess the effects of potential therapeutic interventions on intermediate physiological measures or studies aimed at definitive clinical outcomes. All projects fulfilling these criteria must be submitted through the Clinical Research Program. If there is any doubt about whether a study should be considered to be a Merit Review Program or a Clinical Research Program, application should be made to the Clinical Research Program by letter of intent (LOI) according to the instructions in Attachment A. After LOI review, the applicant will be informed if the proposal should be submitted as a Merit Review Program or a Clinical Research Program. Clinical research proposals that are inappropriately submitted as Merit Review Programs may be returned unreviewed.

b. A typical Clinical Research Program would be for a single-site or small multi-site study with a budget not to exceed $150,000 per year, excluding Principal Investigator salary and equipment, for up to 3 years. It is anticipated that funded studies will produce a definite answer to an intermediate endpoint related to potential therapeutic intervention, produce a definite answer to a clinical question, or lead to a larger clinical trial. In most cases, a study would have at least two comparison subject groups and a clear endpoint. Therefore, Clinical Research awards are not renewable through this program. Phase I (safety) trials are not appropriate for this program.

3. The Clinical Research Program is open to all eligible MRS investigators with permission to submit. New non-clinician Ph.D. investigators, who have not already done so, must obtain permission to submit prior to proposal application.

4. The Clinical Research Program is an exception to the single Merit Review Program rule. An investigator may have a Merit Review Program and a Clinical Research Program at the same time, but an investigator may have only one funded Clinical Research Program. A Clinical Research Program may have only one Principal Investigator.

5. Each applicant is required to submit an LOI by March 1 or September 1 for submission of a full proposal the following June 21 or December 21, respectively.

a. A Request for Exception letter must be included with the LOI package for a proposal requesting any of the following: a budget in excess of $150,000 per year, exclusive of nonclinician Principal Investigator salary and equipment, duration of more than 3 years, or participation of more than one research site. LOIs must be prepared in accordance with the instructions provided in Attachment A.

b. LOI evaluations will be based on scientific merit, including clinical trials methodology. relevance of the problem to the Department of Veterans Affairs (VA) and to the MRS research portfolio, qualifications of the applicant, and cost of the research. Cost-sharing arrangements with other funding sources are encouraged and may be a consideration in the LOI evaluation process. NOTE: Discussion of possible Clinical Research Programs with MRS Program Specialists (121E) prior to LOI submission is strongly encouraged.

6. Full proposals will be accepted from investigators with an approved LOI.

a. All applications must comply with the most recent general guidelines for submitting MRS Merit Review proposals as modified in Attachment B.

b. An application that is disapproved may not be resubmitted. An application that is approved but not funded may be revised and resubmitted only if a resubmission is recommended by the Clinical Research Subcommittee and approved by MRS.

7. Questions about the Clinical Research Program should be directed to Sola Whitehead (x52885), Margaret Doherty (x56620), or Lisa Gunion-Rinker (x54481).

SUGGESTED FORMAT FOR LETTERS OF INTENT FOR THE MEDICAL RESEARCH SERVICE CLINICAL RESEARCH PROGRAM

1. A Letter of Intent (LOI) should consist of single-spaced typed pages. Use only letter-quality print. All text must be prepared with at least 11-point font, with no more than 15 characters per inch, and no more than 6 lines per inch. Page margins must be a minimum of 1 inch at each edge.

2. Each copy of the LOI should include the following materials in the order specified:

a. Department of Veterans Affairs (VA) Form 10-1313-13, VHA Research and Development Letter of Intent Cover Page. In block 1, check Medical Research Service. In block 3, check Response to Specific Announcement and specify Clinical Research Program. In subsequent blocks, provide the title of the project (not to exceed 72 characters including spaces); name of Principal Investigator; VA position title; percent VA effort (8ths,); and the other requested information.

b. The LOI text should be no more than 4 pages and contain the following information:

(1) Objective(s) of the proposed research.

(2) Importance of the study to VA and its patients.

(3) Statements documenting the scientific background and preliminary data that support the viability of the study.

(4) Description of the proposed study design, including the following items:

(a) Study type descriptor: e.g., randomized or non-randomized clinical trial;

(b) Subject recruitment site(s);

(c) Description of base population and intervention or treatment groups to be studied and methods of randomization;

(d) Justification of endpoints to be evaluated, and procedures and links between questions, data, and endpoints;

(e) Data collection methods, intervals, and follow-up procedures;

(f) General analytic plan: statistical analysis, sample size calculations;

(g) Description of the feasibility of completing the study at the proposed site; and

(h) Resources: study duration and estimated annual and total costs with subtotals for personnel, consultants, equipment, supplies, and all other expenses categories.

c. The Principal Investigator should sign the LOI. The Associate Chief of Staff for R&D and the Medical Center Director acknowledge endorsement of the LOI by signing on VA Form 10-1313-13.

d. VA Forms 1313-5, 6, 7, and 8 for the Principal Investigator are to be appended to the LOI.

e. A one-page Request for Exception letter must be appended to any LOI requesting the following: an annual budget request over $150,000, exclusive of non-clinician Principal Investigator salary and equipment, a duration of more than 3 years, or the participation of more than one research facility. Explain why the exception is justified based on the topic, the nature of the study, unusual resource requirements, or other special considerations.

3. LOIs are considered incomplete and may not be reviewed if they are not submitted in accordance with the established procedure.

4. LOI notification of approval grants permission to submit a full proposal during either of the two review cycles immediately following the approval. Resubmission of full proposals is by invitation only.

5. Due Dates. LOIs will be reviewed semi-annually. The deadlines for receipt of LOIs at VA Central Office are March 1st for June 21 proposal submission and September 1st for the December 21 proposal submission. Submit the original LOI plus 10 copies to the following address:

a. If mailed through the U.S. Postal Service, send to:

Clinical Research Program LOI
Medical Research Service
Program Management Division (121E)
VA Central Office
810 Vermont Avenue, NW
Washington, DC 20420

b. LOIs shipped to Medical Research Service by door-to-door couriers such as Federal

Express should be mailed to:
Clinical Research Program LOI
Medical Research Service
Program Management Division (121E)
Department of Veterans Affairs
1400 Eye Street, NW, Suite 400
Washington, DC 20005

INSTRUCTIONS FOR APPLICATIONS
MEDICAL RESEARCH SERVICE CLINICAL RESEARCH PROGRAM

1. Full applications must be complete at the time of submission and must comply with all of the guidelines for submitting Medical Research Service (MRS) Merit Review proposals with the following modifications:

a. A table of contents should be inserted immediately after the abstract.

b. In the personnel section, a statistician to be associated with the project should be identified and the statistician's role should be clearly delineated.

c. The budget should contain a line item for costs of study safety monitoring.

d. The proposal narrative (Rationale, Background and Work Accomplished, and Work Proposed) must contain all figures, tables, and graphs and may be no more than 25 pages. An appendix may be used only for ancillary material such as research data forms, if appropriate. In the narrative, address the following:

(1) In the Background and Work Accomplished section, include references to meta-analysis studies, if appropriate. If the study involves the use of drugs, pertinent pharmacological and toxicological data should be summarized with appropriate documentation.

(2) As appropriate, the following items should be included in the Work Proposed section:

(a) An experimental design of the study, including controls;

(b) A flowchart of basic study design;

(c) Patient recruitment, patient selection criteria, and method of assignment of patients to comparative groups;

(d) Intervention and/or methods of treatment including, if appropriate, provision for double-blinding and breaking the blind;

(e) Methods of follow-up and methods of assuring uniformity of the intervention;

(f) Outcome measurements including any specialized rating scales;

(g) A schedule of observations and laboratory tests;

(h) Sample size issues including the assumptions used to determine number of patients required, duration of patient intake period, number of participating medical centers, and notation of other studies that could compete for patients; and

(i) Statistical analysis section which describes how the major hypothesis or research questions will be tested, including the specification of major endpoints.

e. After the narrative, in a section titled "Safety and Monitoring," the plans for monitoring the safety of participants and the validity and integrity of the data must be detailed. For multi-site projects, describe any quality assurance procedures including plans for auditing or monitoring clinical site practices. A data monitoring board (DMB) equivalent (which may consist of one individual) must be proposed at the time of submission. The responsibility of the DMB is to review the progress of the study for safety and efficacy every 6 months with a recommendation to the local IRB to either continue or terminate the trial. If this report is prepared, a copy is required by Medical Research Service.

f. A copy of the LOI approval letter for the project should be included as the first letter in the Letters of Endorsement section.

2. Due Dates. Proposals will be reviewed semi-annually. The deadlines for receipt of complete proposals at VA Central Office are June 21 and December 21. Submit the original proposal plus 25 copies to the following mailing address:

a. If sent by the U.S. Postal Service, send to:

Program Review Division (121F)
VA Central Office
810 Vermont Avenue, NW
Washington, DC 20420

b. Proposals shipped to Medical Research Service by door-to-door couriers such as Federal Express should be sent to:

Program Review Division (121F)
Department of Veterans Affairs
1400 Eye Street, NW, Suite 700
Washington, DC 20005